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ORIGINAL ARTICLE

The Study of TSH Surge in Apparently Euthyroid Obese Individuals and Its Link to Leptin

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ABSTRACT

Background: There is a complex link between obesity and thyroid hormones. Thyroid Stimulating Hormone (TSH) normally shows a nocturnal surge in euthyroid individuals which, if blunted, may indicate a subtle thyroid dysfunction. Aim: Our target was to study the TSH surge in euthyroid participants with obesity and explore its link with leptin levels.

Methods: We conducted our pilot cross-sectional study on 60 euthyroid obese patients. Patients with primary or secondary hypothyroidism or those taking levothyroxine were excluded. Patients with severe acute illness, depression, renal, hepatic and cardiac disease were also ruled out. For all participants we recorded TSH at 10 am, 7pm, and 10 pm to determine its peak and nadir levels to express the TSH surge as percent rise over nadir [(peak TSH - nadir TSH) × 100] / nadir TSH. TSH surge was considered blunted if below 50 % rise above nadir (normal 50- 300%). Leptin and glucose parameters were investigated.

Results: 13.333% participants had blunted TSH surge with mean TSH at 10 am 4.240± 0.910, 7pm 3.805±0.835 and 10 pm 5.040 ±1.143. All participants were divided into a group with blunted TSH surge and another group with normal TSH surge. Comparing the two groups a significant difference was detected regarding HbA1c not leptin. In patients with a blunted TSH surge, TSH surge was not correlated to leptin yet correlated to HbA1c.

Conclusion: Our study showed that 13.333% of euthyroid obese patients had a blunted TSH surge. Further studies are needed to establish a causal effect relationship.

Key words: TSH surge, obesity, leptin.

INTRODUCTION

The link between obesity and thyroid function operates in two directions and is complex. Disorders of the thyroid can lead to alterations in body weight because thyroid hormones play a central role in regulating heat production and energy intake (1, 2).Over recent decades, evidence has increasingly suggested that obesity itself can trigger modifications in blood levels of thyroid function indicators (3).

Moreover, even subtle shifts in thyroid activity, remaining within the normal reference range, have been implicated in the development of metabolic syndrome. (4–7).The mechanisms driving this relationship are multifaceted and include the impact of adipose tissue on the hypothalamic–pituitary–thyroid (HPT) axis (8).

TSH is reported to show significant circadian periodicity as nocturnal surge, a blunted nocturnal TSH rise could support hidden mild form of thyroid dysfunction (9,10,11).

Obesity can precipitate resistance to Leptin which an important contributor to metabolism (12). **Liu et al 2025** reported that a link exists between leptin and thyroid dysfunction with an intricate relationship between TSH and leptin and highlighted the importance of

considering hormonal and circadian factors in metabolic regulation. (13)

Aim of the work: To study TSH surge in obese patients with apparently euthyroid state and its relation to leptin levels.

METHODS

Our pilot cross-sectional study was conducted at Ain Shams University hospital with participants recruited from the diabetes and endocrinology outpatient clinics . Informed written consent was obtained together with the approval of the research ethics committee at Faculty of Medicine Ain Shams University MD132/2015. We included 60 middle aged adults with a body mass index above 30 kg/m2 and a normal TSH, Free Thyroxine (FT4) and Free Triiodothyronine (FT3). We excluded participants with renal, hepatic and cardiac disease, severe acute illness or depression and those individuals on anti-psychotics , anti-depressants and contraception.

Patients known to have primary or secondary hypothyroidism or taking levothyroxine replacement were also excluded.

All participants were subjected to full history taking with full clinical evaluation. We measured TSH measurement by ELISA at 10 am, 7 pm and 10 and calculated TSH surge as follows: [(peak TSH - nadir TSH) × 100] / nadir TSH. TSH surge was expressed as a percentage rise over nadir. TSH surge values 50- 300% rise above nadir was considered normal and less than 50% was considered blunted .

Laboratory tests included serum leptin using DRG Leptin ELISA (an enzyme immunoassay for the quantitative in vitro diagnostic measurement of leptin in serum).We also measured FPG, 2hPP, HbA1c, lipid profile, renal and liver functions.

All data was entered into an IBM compatible PC on MS Excel spread sheet. Analysis was done using SPSS package system V. 17. Description of quantitative variables was done in the form of mean and SD. Description of qualitative variables was in the form of frequency and percentages. Unpaired Student T-test and Chi-square were used to compare between two groups in quantitative data and qualitative data respectively. Pearson correlation coefficient was used to detect the correlation between two quantitative parameters in the same group. We considered p value significant when less than 0.05.

RESULTS

Descriptive data of all participants

Participants had a mean age of 42.217±5.723 years, 50% of them were males. They also had a mean BMI 32.028±1.338 kg/m2, TSH Surge was 183.557± 180.702 % Mean Leptin was 4.010±2.257 ng/ml ,mean HbA1c 6.320±1.361 %, mean FPG 131.467±36.860 mg/dl and mean 2hpp of 194.083±44.465 mg/dl. As regards lipid profile they had a mean of total cholesterol 209.26±49.498 mg/dl, mean LDL 113.083±20.840 mg/dl, mean HDL 47.733±5.851 mg/dl and mean Triglycerides 165.083±16.282 mg/dl. (Table 1).

we divided all subjects in the study into two groups, A group with blunted TSH surge with total number 8 out of 60 (13.333%) and another group of normal TSH surge response with total number 52 out of 60 (86.666%)

In patients with normal TSH surge, mean TSH at 10 am was 3.030±1.135**,** at 7pm 2.270±0.817 and at 10 pm 4.770±1.030 Table1 Figure 1 In patients with a blunted TSH surge, mean TSH at 10 am was 4.240± 0.910 mIU/L**,** at 7pm 3.805±0.835 mIU/L and at 10 pm 5.040 ±1.143 mIU/L (Figure 2)

Statistical analysis:

Comparison of participants with blunted and non-blunted TSH surge

On comparison between TSH surge blunted response group and non-blunted response group there was a significant difference as regards HbA1C, total cholesterol and LDL yet no difference between age, leptin, BMI, FPG, 2hPP, TGs and HDL (Table 2).

In patients with a blunted TSH surge each of TSH surge and leptin was negatively correlated with HbA1C. They showed no correlation between each other and with BMI, FPG, 2hPP, total cholesterol, LDL, TG and HDL (Table 3).

In patients with a normal TSH surge, TSH surge and leptin were not correlated to each other or with any of BMI, HbA1C, FBS, 2hPP, total cholesterol, LDL, TGs and HDL (Table 4).

Table 1: descriptive data all participants.

Descriptive Data						
	Range			Mean	±	SD
Age (years)	33	-	54	42.217	±	5.723
BMI kg/m2	30.1	-	35.3	32.028	±	1.338
TSH Surge%	20	-	763	183.557	±	180.702
Leptin ng/ml	0.7	-	10.5	4.010	±	2.257
HbA1c%	4.1	-	9	6.320	±	1.361
FPG mg/dl	72	-	188	131.467	±	36.860
2hpp mg/dl	114	-	295	194.083	±	44.465
TG mg/dl	124	-	198	165.083	±	16.282
HDL mg/dl	33	-	65	47.733	±	5.851
LDL mg/dl	85	-	175	113.083	±	20.840
TC mg/dl	145	-	393	209.267	±	49.498
	Male			Female		
Gender	30	(50%)		30	(50%)	

Table 2: Comparison between patients with blunted and non-blunted TSH surge as regards different study parameters.

	TSH Surge						T-Test	
	Blunted			Non-Blunted				
	Mean	±	SD	Mean	±	SD	t	P-value
Age (years)	42.714	±	7.064	44.182	±	5.053	0.651	0.519
BMI kg/m2	32.743	±	1.555	31.945	±	1.401	-1.343	0.187
Leptin ng/ml	3.614	±	1.663	4.536	±	2.721	0.858	0.396
FPG (mg/dl)	149.571	±	28.739	155.121	±	19.455	-0.629	0.533
2hpp (mg/dl)	230.714	±	53.565	211.788	±	32.554	-1.240	0.223
HbA1c %	7.586	±	1.165	6.900	±	1.078	-1.509	0.012*
TG (mg/dl)	170.286	±	10.563	164.061	±	13.474	-2.986	0.264
HDL (mg/dl)	45.857	±	6.012	47.576	±	5.494	0.740	0.464
LDL(mg/dl)	140.714	±	35.146	111.848	±	14.866	-3.553	0.001*
TC (mg/dl)	293.714	±	81.918	205.242	±	32.321	-4.828	<0.001*

Table 3: Correlation of TSH surge and different study parameters in patients with blunted TSH surge

		TSH Surge	
		r	P-value
	BMI kg/m2	-0.583	0.170
Patients with blunted TSH surge	Leptin ng/ml	0.083	0.860
	HbA1c %	-0.228	0.010*
	FPG (mg/dl)	-0.340	0.456
	2hpp (mg/dl)	-0.455	0.305
	TG (mg/dl)	-0.330	0.470
	HDL (mg/dl)	0.339	0.456
	LDL (mg/dl)	-0.485	0.270
	TC (mg/dl)	-0.554	0.197

Table 4: Correlation of TSH surge with different study parameters in patients with non-blunted TSH surge

		TSH Surge	
		r	P-value
	BMI kg/m2	-0.121	0.503
Patients with non-blunted TSH surge	Leptin ng/ml	0.130	0.469
	HbA1c%	-0.440	0.623
	FPG (mg/dl)	-0.046	0.801
	2hpp (mg/dl)	-0.089	0.621
	TG (mg/dl)	-0.105	0.561
	HDL (mg/dl)	0.088	0.627
	LDL (mg/dl)	-0.114	0.528
	TC (mg/dl)	-0.004	0.982

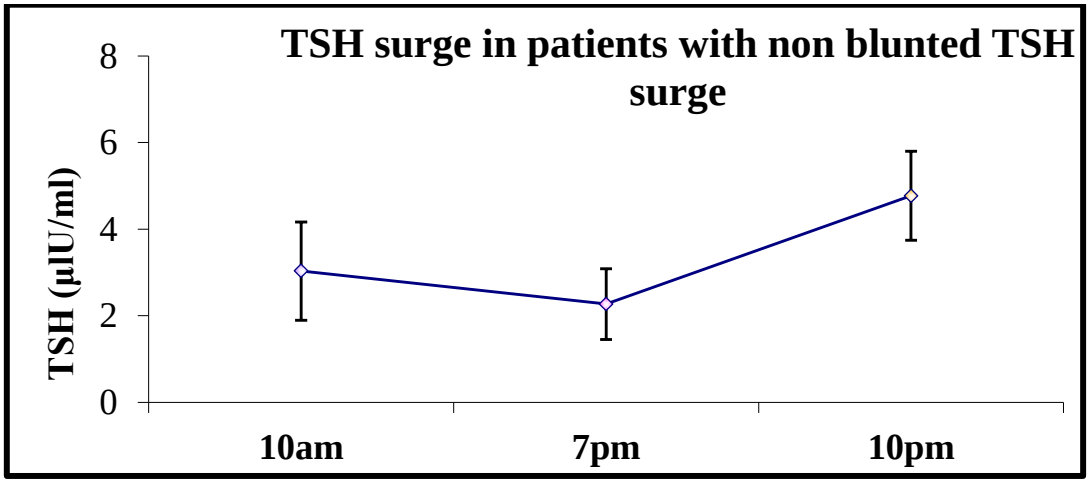

Figure 1: Pattern of TSH surge in patients with non-blunted TSH surge.

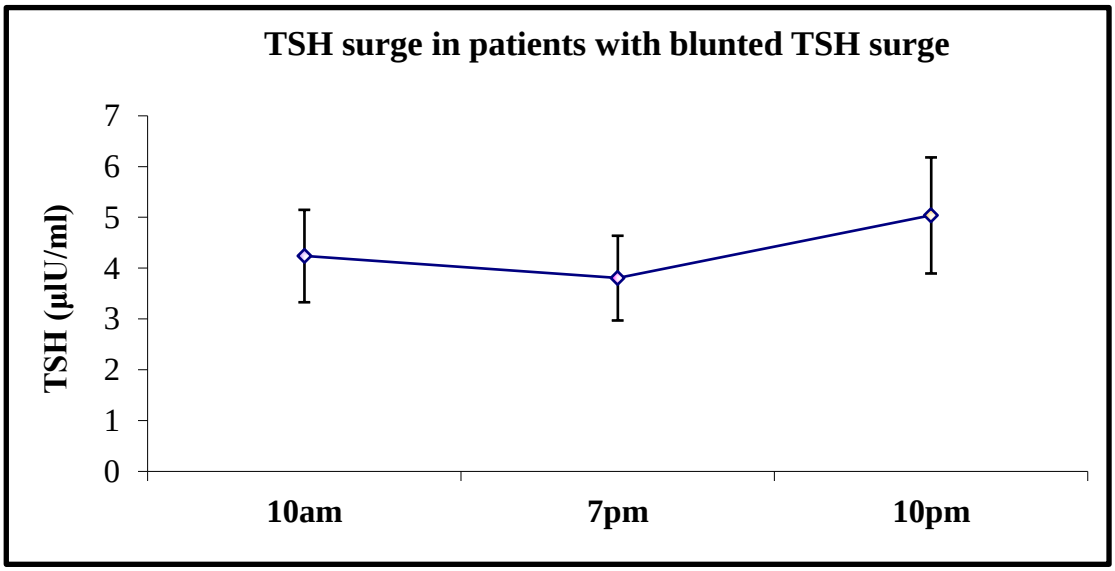

Figure 2: Pattern of TSH surge in patients with blunted TSH surge.

DISCUSSION

The hypothalamic-pituitary–thyroid axis is controlled by the circadian clock through the suprachiasmatic nucleus pacemaker .Chronic circadian disruption has long-term consequences contributing to the risk of obesity, type 2 diabetes mellitus(T2DM) (21) .In our work we demonstrated that 8 patients of the 60 euthyroid obese participants (13.333%) had a blunted TSH surge with mean TSH at 10 am 4.240± 0.910 mIU/L, at 7pm 3.805±0.835 mIU/L and at 10 pm 5.040 ±1.143 mIU/L.The overall mean TSH in an obese euthyroid cohort studied by mele et al was 2.08 ± 1.20 mIU/L (14) The interplay between obesity and thyroid function is bidirectional, with thyroid hormones influencing energy balance and body weight, while excess adiposity can, in turn, alter circulating thyroid markers. Even variations in thyroid activity within the normal range have been linked to metabolic disturbances such as visceral obesity, dyslipidaemia, insulin resistance, and hypertension, possibly through adipose tissue effects on the HPT axis. (14)

Obesity can precipitate resistance to Leptin which an important contributor to metabolism and has a considerable effect on glucose levels by activating the hypothalamic JAK2/STAT3 signalling pathway (12)

Liu et al 2025 reported an association of higher leptin and hypothyroidism supporting a link between leptin and thyroid dysfunction. (13) In our work on comparing participants with and without blunted TSH surge, no significant difference as regards leptin was detected. Additionally, TSH surge and leptin showed no correlation between each other in both groups. Our results do not support the link between blunted TSH surge and leptin. **Mantzoros. et al (2001)**, who studied the link between diurnal changes of both leptin and TSH, supported a relationship between hypothalamic-pituitary-thyroid axis fluctuations in circulating TSH and leptin (15) which was different from our findings. This could be due to measuring only basal leptin in our work rather than over 24 hours.

In our study, in patients with a blunted TSH surge, the TSH surge was negatively correlated with HbA1C. There was a significant difference as regards HbA1C on comparing groups with and without TSH surge blunted surge. Our findings support that thyroid function is linked to glucose homeostasis and metabolism and that checking and managing thyroid health may be important for preventing or treating conditions like insulin resistance and DM (16).

Hypothyroidism is linked to glucose intolerance and insulin resistance and upon adequate replacement of thyroid hormones the insulin sensitivity improves (17-19). Mild degrees of hypothyroidism showed deterioration of glucose metabolism and

adequate management of these mild forms of hypothyroidism may improve the condition and decrease the risk of prevent cardiovascular morbidities (9,20).Thyroid hormones increase the number of glucose transporters on the cell surface of myocytes playing an important role in their glucose uptake (21).Thyroid dysfunction, particularly hypothyroidism, increases insulin resistance in muscle and fat tissue. (22, 23) This happens due to impaired movement of glucose transporters to the cell surface, disrupted leptin signaling, and higher levels of free fatty acids—all of which reduce glucose uptake by muscle cells and worsen blood sugar control (22).

Exploring how TSH levels change throughout the day in obese people with normal thyroid function can help us understand more about how their bodies work. Even though their thyroid tests come back normal, obesity might still affect how TSH is released—especially its daily rhythm and timing.

This matters because small changes in TSH patterns could be linked to how the body handles weight and metabolism. If we only check TSH once in the morning, we might miss important shifts that happen at night. That could lead to misreading someone's thyroid health or missing early signs of hormonal imbalance.

Also, not all obese individuals have the same health risks. Studying TSH rhythms might help us tell the difference between those who are metabolically healthy and those who aren't. This could lead to more personalized treatments and better ways to manage obesity.

Future studies should look at whether changing TSH rhythms—through sleep, diet, or medication—can improve health outcomes. It would also be useful to track these patterns over time to see if they play a role in developing obesity-related problems.

Limitations:

The pilot cross-sectional study nature in middle-aged euthyroid obese individuals, limits causal inference and generalizability. Although age group is relatively homogeneous, compared to younger or elderly populations, a larger sample and narrower age band would add precision. As our aim was to assess TSH surge variability within obese individuals, no normal-BMI control was included; future studies should address this.

Conclusion: A noticeable percentage of euthyroid obese patients had a blunted TSH surge which could indicate a subtle thyroid dysregulation in these patients. We did not find a link between blunted TSH surge and leptin yet a correlation with HbA1c was found. Our study opens the way for further studies to confirm the link between disrupted TSH rhythm and obesity.

Disclosures:

Conflicts of interests: The authors report no conflicts of interests.

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Ethical considerations: The research ethics committee at Faculty of Medicine Ain Shams University approved the study with issue and date: MD132/2015

Data availability: Available on request

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REFERENCES

1. Iwen KA, Oelkrug R, Brabant G. Effects of thyroid hormones on thermogenesis and energy partitioning. J Mol Endocrinol (2018) 60:R157–70. doi: 10.1530/JME-17-0319

2. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev (2014) 94:355–82. doi: 10.1152/physrev.00030.2013

3-Pearce EN. Thyroid hormone and obesity. Curr Opin Endocrinol Diabetes Obes (2012) 19:408–13. doi: 10.1097/MED.0b013e328355cd6c

4. Xu R, Huang F, Zhang S, Lv Y, Liu Q. Thyroid function, body mass index, and metabolic risk markers in euthyroid adults: A cohort study. BMC Endocr Disord (2019) 19:58. doi: 10.1186/s12902-019-0383-2

5. Roef GL, Rietzschel ER, Van Daele CM, Taes YE, De Buyzere ML, Gillebert TC, et al. Triiodothyronine and free thyroxine levels are differentially associated with metabolic profile and adiposity-related cardiovascular risk markers in euthyroid middle-aged subjects. Thyroid (2014) 24:223–31. doi: 10.1089/thy.2013.0314

6. Liu Y, Wang W, Yu X, Qi X. Thyroid function and risk of non-alcoholic fatty liver disease in euthyroid subjects. Ann Hepatol (2018) 17:779–88. doi: 10.5604/01.3001.0012.3136

7. Wolffenbuttel BHR, Wouters HJCM, Slagter SN, van Waateringe RP, Muller Kobold AC, van

Vliet-Ostaptchouk JV, et al. Thyroid function and metabolic syndrome in the population-based LifeLines cohort study. BMC Endocr Disord (2017) 17:65. doi: 10.1186/s12902-017-0215-1
8. Seoane LM, Carro E, Tovar S, Casanueva FF, Dieguez C. Regulation of in vivo TSH secretion by leptin. Regul Pept (2000) 92:25–9. doi: 10.1016/S0167-0115(00)00145-2
9- Luca Persani, Biagio Cangiano, and Marco Bonomi. 2019.The diagnosis and management of central hypothyroidism in.Endocrine Connections(2018) Volume 8: Issue 2 R44–R54.
10- Vanhaelst L, Van Cauter E, Degaute JP, Golstein J. Circadian variations of serum thyrotropin levels in man. J Clin Endocrinol Metab(1972) 35: 479–82.
11- Greenspan SL, Klibanski A, Schoenfeld D, Ridgway EC .1986. Pulsatile secretion of thyrotropin in man. J Clin Endocrinol Metab 63: 661–8.
12- Prashanjit Roy , Rishi Kant , Amandeep Kaur , Hardik Kumar , Ranjeet Kumar Leptin Resistance and Cardiometabolic Disorders: Bridging Molecular Pathways, Genetic Variants, and Therapeutic Innovation. Curr Cardiol Rev (2025). doi: 10.2174/011573403X356019250118170444.
13. Liu S, Ma J, Zhang L, Yang Y, Han Z , Tian L. . Circulating leptin levels in thyroid dysfunction: a systematic review and meta-analysis. BMC Endocrine Disorders (2025) volume 25, Article number:140.
14-Chiara Mele, Stefania Mai, Tiziana Cena, Loredana Pagano, Massimo Scacchi, Bernadette Biondi, Gianluca Aimaretti, Paolo Marzullo. The pattern of TSH and fT4 levels across different BMI ranges in a large cohort of euthyroid patients with obesity. Front. Endocrinol., (2022) Volume 13
15. Mantzoros C.S., Ozata M., Negrao A. B. et al.. Synchronicity of Frequently Sampled Thyrotropin (TSH) and Leptin Concentrations in Healthy Adults and Leptin-Deficient Subjects: Evidence for Possible Partial TSH Regulation by Leptin in Humans The Journal of Clinical Endocrinology and Metabolism (2001) 86(7):3284-91
16. Gu Y, Li H, Bao X, Zhang Q, Liu L, Meng G, et al. The relationship between thyroid function and the prevalence of type 2 diabetes mellitus in euthyroid subjects. J Clin Endocrinol Metab. (2017)102:434–42.
17.Duntas LH, Orgiazzi J, Brabant G. 2011. The interface between thyroid and diabetes mellitus. Clin Endocrinol (Oxf) 75:1–9.
18.Chaker L, Ligthart S, Korevaar TI, Hofman A, Franco OH, Peeters RP, et al. Thyroid function and risk of type 2 diabetes: a population-based prospective cohort study. BMC Med. (2016) 14:150.
19. Joffe BI, Distiller LA. Diabetes mellitus and hypothyroidism: strange bedfellows or mutual companions? World J Diabetes. (2014) 5:901–4.
20.Han C, He X, Xia X, Li Y, Shi X, Shan Z, et al.Subclinical hypothyroidism and type 2 diabetes: a systematic review and meta-analysis. (2015) PLoS One10: e0135233.
21. Lambadiari V, Mitrou P, Maratou E, Raptis AE, Tountas N, Raptis SA, et al. Thyroid hormones are positively associated with insulin resistance early in the development of type 2 diabetes. Endocrine (2011) 39:28–32.
22. Biondi B, Kahaly GJ, Robertson RP..Thyroid dysfunction and diabetes mellitus: two closely associated disorders. Endocr Rev. (2019) 40:789–824.
23. Kalra S, Aggarwal S, Khandelwal D. Thyroid dysfunction and type 2 diabetes mellitus: screening strategies and implications for management. Diabetes Ther. (2019)10:2035–44.

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